



domain of the mature c-MET protein and spans amino acids 24-306 of SEQ ID NO.

12. The  $\beta$  chain would consist of 1,084-5 amino acids with the predicted  $\beta$  chain extracellular domain being amino acids 306 to 932, the single transmembrane hydrophobic segment being amino acids 933 to 955, and the intracellular domain being amino acids 956 to 1390 of SEQ ID NO 12.--

Please delete the paragraph beginning at page 78, line 3, and substitute therefor the following replacement paragraph:

--Intravascular injection may be by intravenous or intraarterial injection: carotid artery injection is thought to assist in administration to the brain, and is thus preferred. Antibody-agents injected into the blood stream have been shown to cross the blood-brain barrier and to infiltrate the cranial cavity to some extent, usually in the range of  $10^{-4}$  to  $10^{-3}\%$  injected dose per gram. This rate of uptake may be sufficient for imaging reagents, and also may be useful for tumor cell specific cytotoxic agents (e.g, those specifically directed to the inhibition of the function of tumor-cell overexpressed proteins). However, in order to achieve therapeutic concentrations of the antibody-therapeutic agents without unacceptable toxicity to the patient, it is preferred that the therapeutics compositions be administered by intrathecal injection, direct injection, or injection into the cerebro-spinal fluid.--

A marked-up version of the aforementioned paragraphs are attached hereto as Appendix "A".

Applicant believes that no fees are due in connection herewith. However, the Commissioner is authorized to charge counsel's Deposit Account No. 12-2475 for any fee deficiencies found to be associated with this filing.

Respectfully submitted,

**LYON & LYON LLP**

Dated: November 1, 2001

By: 

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